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10/602,692	06/20/2003	Jean-Pierre Sommadossi	06171.IDX 1006 CON3	1379

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EXAMINER

MCINTOSH III, TRAVISS C

ART UNIT

PAPER NUMBER

1623

DATE MAILED: 04/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/602,692

Applicant(s)

SOMMADOSSI ET AL

Examiner

Traviss C. McIntosh

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 March 2004.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 89 and 130-158 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 89 and 130-158 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 20 June 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____

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Detailed Action

The preliminary amendment filed 6/20/03 has been received and the specification and claims have been amended as requested.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on March 9, 2004 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 89 and 130-158 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 89 and 130-153 of copending Application No. 10/602,976. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications are drawn to treating

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members of the Flaviviridae family with the same compounds. It is known that HCV is a member of the genus hepacivirus, and that hepacivirus, flavivirus, and pestivirus make up the family Flaviviridae, therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to treat flavivirus, pestivirus, and HCV with the same compounds.

Claim Objections

Claim 158 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 158 states that the flavivirus or pestivirus of claim 89 is not a hepatitis C virus, however, hepatitis C virus is not a flavivirus or pestivirus, and thus claim 158 adds nothing to the patentability of claim 89 as claim 89 is still drawn to treating only a flavivirus or pestivirus and therefor hepatitis C virus (HCV) is already delimited from claim 89. It is noted that HCV is a member of the genus hepacivirus, and since HCV is not a flavivirus or pestivirus, claim 158 is not seen to be limiting to claim 89.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 89 and 130-158 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating flavivirus and pestivirus infections using compounds in which R¹ and R² are H; phosphate; a stabilized phosphate prodrug; acyl; alkyl; sulfonate ester; or benzyl, does not reasonably provide enablement for the use of compounds wherein R¹ and R² are lipids; amino acids; carbohydrates; peptides; cholesterol; or other pharmaceutically acceptable leaving groups which when administered *in vivo* are capable of providing a compound wherein R¹ and R² are H or phosphate. Additionally, the specification is seen to be enabling for using compounds wherein R⁶ is lower alkyl and wherein R⁷ is not H, but is not seen to be enabling for using compounds wherein R⁶ is any of the remaining moieties claimed or wherein R⁷ is H. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Undue experimentation is a conclusion reached by weighing the noted factual considerations set forth below as seen in *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). A conclusion of lack of enablement means that, based on the evidence regarding a fair evaluation of an appropriate combination of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

These factors include:

- (A) The breadth of the claims;
- (B) The nature of the invention;
- (C) The state of the prior art;
- (D) The level of one of ordinary skill;
- (E) The level of predictability in the art;
- (F) The amount of direction provided by the inventor;
- (G) The existence of working examples; and

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- (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims - The nature of the invention

Claim 89 is drawn to a method of treating a flavivirus or pestivirus in a host by administering the compound of claim XVII. Claims 130-141 limit various moieties of the compound of formula XVII of claim 89. Claims 142-146 are drawn to combination therapy using the compound of claim 89. Claims 147-153 limit the formulations used in the method of claim 89. Claims 154-158 limit the viruses treated in claim 89.

The state of the prior art

Modified nucleosides are known in the art to be useful in the treatment of HCV, flavivirus, and pestivirus wherein the modifications can occur on the sugar and the base, as seen by Ismaili et al. (US Patent 6,784,161). Substitutions known to occur at the R¹, R¹⁰, R⁹, and R⁷ position of the instant compound are known to be various moieties, including phosphates; acyl; alkyl; ester; or benzyl groups, as seen by Ismaili et al. The art is silent to the use of any lipids; amino acids; carbohydrates; peptides; cholesterol; or other pharmaceutically acceptable leaving groups which when administered *in vivo* are capable of providing a compound wherein R¹ and R² are H or phosphate. Additionally, the art is silent to the use of 2'-di-substituted nucleosides for treating viral infections.

The level of predictability in the art

The examiner acknowledges the probability and predictability that the active agent, being a compound of formula XVII having a lower alkyl group in the R⁶ position wherein R⁷ is not H, as well as having the claimed moieties other than lipids; amino acids; carbohydrates; peptides;

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cholesterol; or other pharmaceutically acceptable leaving groups which when administered *in vivo* are capable of providing a compound wherein R^1 and R^2 are H or phosphate in the R^1 and R^2 position, indeed have efficacy as instantly asserted.

The amount of direction provided by the inventor

The instant specification is not seen to provide adequate guidance which would allow the skilled artisan to extrapolate from the disclosure and examples provided to use the claimed method commensurate in the scope with the instant claims. There is a lack of data and examples which adequately represent the scope of claim as written. The examiner notes, there has not been provided sufficient instruction or sufficient methodological procedures to support the alleged efficacy instantly asserted using a compound from the broad group of claim 89. There is no teaching of how to make compounds with the various lipids; amino acids; carbohydrates; peptides; cholesterol; or other pharmaceutically acceptable leaving groups in the R^1 and R^2 positions.

The existence of working examples

The working examples set forth in the instant specification are directed to the use of 2'-CH₃-ribo-nucleic acids in viral assays. There are no examples of any compounds used comprising lipids; amino acids; carbohydrates; peptides; cholesterol; or other pharmaceutically acceptable leaving groups in the R^1 or R^2 positions. There are also no examples of any compounds used comprising molecules other than CH₃ in the R^6 position and OH in the R^7 position.

The quantity of experimentation needed to make and use the invention based on the content of the disclosure

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Indeed, in view of the information set forth supra, the instant disclosure is not seen to be sufficient to enable the use of any compound of claim 89 in the treatment of flavivirus and pestivirus infections without undue experimentation. One skilled in the art could not use the entire scope of the claimed invention without undue experimentation. One skilled in the art would be confronted with an undue burden of experimentation to isolate, characterize, and test the various compounds of claim 89 to determine if indeed they have efficacy as asserted.

As set forth supra, the examiner believes applicants have support for treating flavivirus and pestivirus infections using compounds in which R^1 and R^2 are H, phosphate, a stabilized phosphate prodrug, acyl, alkyl, sulfonate ester, or benzyl; and wherein R^6 is lower alkyl and R^7 is not H.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 89 and 130-158 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 89 R^1 and R^2 are defined as optionally being "benzyl, wherein the phenyl group is optionally substituted with one or more substituents". In the absence of the identity of moieties which are intended to be substituted, thus modifying an art recognized chemical core, described structurally or by chemical name, the identity of "substituted" would be difficult to ascertain. In the absence of said moieties, the claims containing the term "substituted" are not described

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sufficiently to distinctly point out that which applicant intends as the invention. All claims that include the limitation of "substituted" without clearly indicating the moieties which are intended to be substituted, are indefinite.

All claims which depend from an indefinite claim are also indefinite. *Ex parte Cordova, 10 U.S.P.Q. 2d 1949, 1952 (P.T.O. Bd. App. 1989).*

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. US 6,063,628 (Loeb et al.) which teaches modified bases of a ribonucleoside in viral treatment (see column 3, bottom paragraph). US 6,784,161 (Ismaili et al.) which teaches of modified ribonucleosides in viral treatment, as well as combination therapy using the same.

Conclusion


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Traviss C. McIntosh whose telephone number is 571-272-0657. The examiner can normally be reached on M-F 9:30-6:00.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Traviss C. McIntosh
March 31, 2005

 James O. Wilson
Supervisory Patent Examiner
Art Unit 1623


BRUCK KIFLE, PH.D.
PRIMARY EXAMINER